REMARKS

No amendments have been made herein. Claim 4 is canceled. Claims 7-11 are withdrawn. Thus, Claims 1, 2 and 5 are presented for further consideration. Applicants have carefully considered all of the Examiner's rejections but respectfully submit that the claims are allowable for at least the following reasons.

Rejections under 35 U.S.C. § 112, first paragraph

The Examiner has rejected Claim 4 under 35 U.S.C. § 112, first paragraph allegedly because the specification does not enable a method of inhibiting calcium T-channel activity with a prodrug of a T-channel antagonist of Formula I. Without acquiescing and solely to advance prosecution, Claim 4 is canceled, thereby rendering its rejection moot.

The Examiner has also rejected Claims 1, 2, 5, and 7-11 under 35 U.S.C. § 112, first paragraph allegedly because the specification "does not reasonably provide enablement for a method of inhibiting calcium T-channel activity with the title T-channel antagonist of Formula I and the derivatives of claim 5." *Office Action* at page 6.

Applicants disagree. First, the Examiner actually acknowledged that Claims 1, 2, and 5 are enabled by stating that the "specification, while being enabling for a method of inhibiting calcium T-channel activity with a T-channel antagonist of Formula I," is not enabling for a prodrug thereof as recited in canceled Claim 4. *Id.* at pages 3-4. (emphasis added)

However, the Examiner contradicted this acknowledgment by arguing that "the specification, while being enabling for methods as described in the Examples of pages 40-71, does not reasonably provide enablement for a method of inhibiting calcium T-channel activity with the title T-channel antagonist of Formula I and the derivatives of claim 5." *Id.* at page 6. The Examiner goes on to emphasize that the presence of working examples in the specification is not sufficient to support the claims because the explicit limitations of claim 1 are nowhere represented throughout the examples. *Id.* at pages 7-8. In particular, the Examiner asserts that Examples 1-50 do not show any reference of T-channel inhibition and even though Examples 48-50 are drawn to expression of T-type channels in mammalian cells, block studies, and animal studies, they are not commensurate in scope with the limitations of Claims 1 and 5. *Id.* at page 8. The Examiner concludes that Examples 1-50 lack data or cumulative results in order to show a

scope of enablement for the method of administration for claims 1 and 5 and that the quantity of experimentation necessary cannot be adequately determined. *Id.*

Applicants point out that the Examiner erroneously has not considered the disclosure of the entire specification and therefore has failed to provide a reasonable basis to question the specification's enabling disclosure. It is well established that "[i]n order to make a rejection, the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. *In re Wright*, 999 F.2d 1557, 1562 (Fed. Cir. 1993), MPEP § 2164.04. Here, the Examiner has overlooked the data actually disclosed in the specification.

In particular, paragraph [0098] of the specification provides time constant data which shows that compounds of Formula I exhibited a long time constant (in the order of minutes) to achieve blockage of current and thus have a slow onset. Moreover, the Examiner has not appreciated the *in vivo* data disclosed in paragraphs [0101] and [0102], and Figures 1 and 2 of the specification. The *in vivo* results corroborate the time constant data and demonstrate that a compound of Formula I (e.g. PPK5) dropped and maintained the reduced systolic pressure past 24 hours in a rat model for hypertension. These results are presented in Figures 1 and 2 of the specification, demonstrating that the onset of activity and duration of activity of the Formula I compound *in vivo* establishes suitability for administration in regular doses no more often than once per day as featured in the instant claims. These data are an actual reduction to practice of the features of Claims 1, 2, and 5 and prove that the specification enables the scope of these claims.

Contrary to the Examiner's conclusion that the quantity of experimentation cannot be determined, the specification provides more than sufficient guidance to a person of ordinary skill in the art for practicing the claimed invention without undue experimentation. In fact, the Examiner has already acknowledged that the specification is enabling for methods of expressing T-type channels in mammalian cells, performing time constant block studies, and testing compounds *in vivo* for anti-hypertensive effects. *Id.* at page 6 ("the specification...being enabling for methods as described in the Examples of pages 40-71") (emphasis added). Indeed, the detailed protocols for expressing T-channels, measuring time constant block, and testing for *in vivo* anti-hypertensive effects are disclosed in working Examples 48-50, which belong to the portion of the specification the Examiner states is enabling.

Based on the foregoing, the Examiner has not satisfied his initial burden of providing a reasonable basis to question the enabling disclosure of the claimed invention. The instant claims relate to methods, not compounds *per se*, and the specification provides detailed teaching of how to make the compounds and test them in thoroughly described *in vitro* assays and an *in vivo* model for hypertension. Moreover, these protocols described in the specification can be readily performed by a person of ordinary skill in the art without undue experimentation. Even though quantity of experimentation is not dispositive of whether claims are enabled, the quantity of experimentation required to perform the assays disclosed in the specification is relatively modest, given the protocols set forth therein.

As such, the specification more than adequately enables the scope of Claims 1, 2, and 5. This conclusion is compelled according to MPEP § 2164.04, which states, "A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph..." (emphasis added). Accordingly, Applicants request withdrawal of the rejection of Claims 1, 2, and 5 under 35 U.S.C. § 112, first paragraph.

CONCLUSION

Applicants have endeavored to respond to each of the rejections in the outstanding Office Action. In light of the above arguments it is believed that the present application is in immediate condition for allowance. If any questions remain that may be resolved over the telephone the Examiner is hereby invited to telephone the undersigned directly as the number below.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicants are not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicants reserve the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure,

including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that Applicants have made any disclaimers or disavowals of any subject matter supported by the present application.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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Dated: November 22, 2010

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